

10/004, 571R>

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NEWS	1	Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	"Ask CAS" for self-help around the clock
NEWS	3 SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4 OCT 28	KOREAPAT now available on STN
NEWS	5 NOV 30	PHAR reloaded with additional data
NEWS	6 DEC 01	LISA now available on STN
NEWS	7 DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8 DEC 15	MEDLINE update schedule for December 2004
NEWS	9 DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10 DEC 17	COMPUBAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11 DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12 DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13 DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14 DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15 DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16 JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17 FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18 FEB 10	STN Patent Forums to be held in March 2005
NEWS	19 FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20 FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21 FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22 FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23 MAR 02	GBFULL: New full-text patent database on STN
NEWS	24 MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	25 MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS EXPRESS		JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
NEWS HOURS		STN Operating Hours Plus Help Desk Availability
NEWS INTER		General Internet Information
NEWS LOGIN		Welcome Banner and News Items
NEWS PHONE		Direct Dial and Telecommunication Network Access to STN

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NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \*

FILE 'HOME' ENTERED AT 17:05:55 ON 08 MAR 2005

=> file reg COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 17:06:01 ON 08 MAR 2005  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 MAR 2005 HIGHEST RN 843607-47-6  
DICTIONARY FILE UPDATES: 6 MAR 2005 HIGHEST RN 843607-47-6

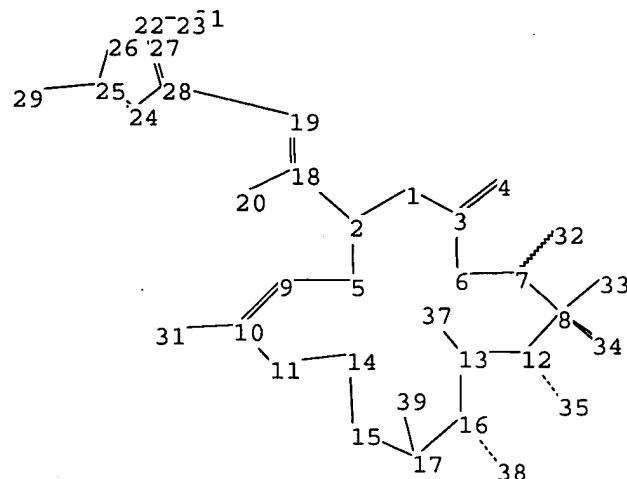
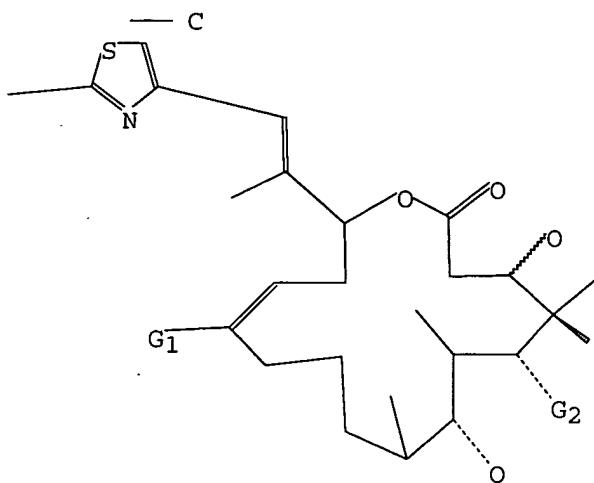
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>  
Uploading C:\Program Files\Stnexp\Queries\10004571.str



chain nodes :

4 18 19 20 21 22 23 29 31 32 33 34 35 37 38 39

ring nodes :

1 2 3 5 6 7 8 9 10 11 12 13 14 15 16 17 24 25 26 27 28

chain bonds :

2-18 3-4 7-32 8-33 8-34 10-31 12-35 13-37 16-38 17-39 18-19 18-20 19-28  
22-23 25-29

ring bonds :

1-2 1-3 2-5 3-6 5-9 6-7 7-8 8-12 9-10 10-11 11-14 12-13 13-16 14-15  
15-17 16-17 24-25 24-28 25-26 26-27 27-28

exact/norm bonds :

3-4 7-32 10-31 12-35 16-38 24-25 24-28

exact bonds :

1-2 1-3 2-5 2-18 3-6 5-9 6-7 7-8 8-12 8-33 8-34 9-10 10-11 11-14  
12-13 13-16 13-37 14-15 15-17 16-17 17-39 18-19 18-20 19-28 22-23 25-26  
25-29 26-27 27-28

isolated ring systems :

containing 1 : 24 :

G1:H,Ak

G2:H,O

Match level :

1:Atom 2:Atom 3:Atom 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS  
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom  
29:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 37:CLASS 38:CLASS  
39:CLASS

Stereo Bonds:

34-8 (Single Hash).

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Stereo Chiral Centers:

8 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 8

L1 STRUCTURE UPLOADED

=> s 11  
SAMPLE SEARCH INITIATED 17:06:29 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 68 TO ITERATE

100.0% PROCESSED 68 ITERATIONS ( 4 INCOMPLETE) 4 ANSWERS  
SEARCH TIME: 00.00.01

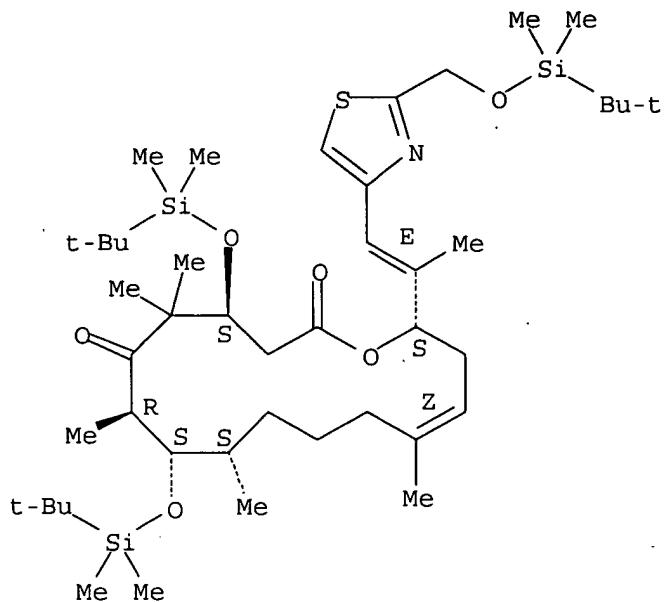
FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 866 TO 1854  
PROJECTED ANSWERS: 4 TO 200

L2 4 SEA SSS SAM L1

=> d scan

L2 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN  
ITERATION INCOMPLETE  
IN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[[(1,1-  
dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-  
dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazoly]-1-methylethenyl]-  
5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI)  
MF C45 H83 N O6 S Si3

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

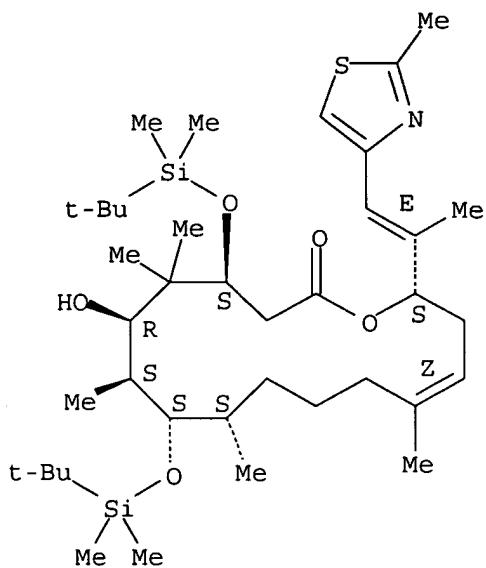
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L2 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN  
ITERATION INCOMPLETE

IN Oxacyclohexadec-13-en-2-one, 4,8-bis[[((1,1-dimethylethyl)dimethylsilyl)oxy]  
]-6-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,6R,7S,8S,9S,13Z,16S)- (9CI)

MF C39 H71 N O5 S Si2

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.

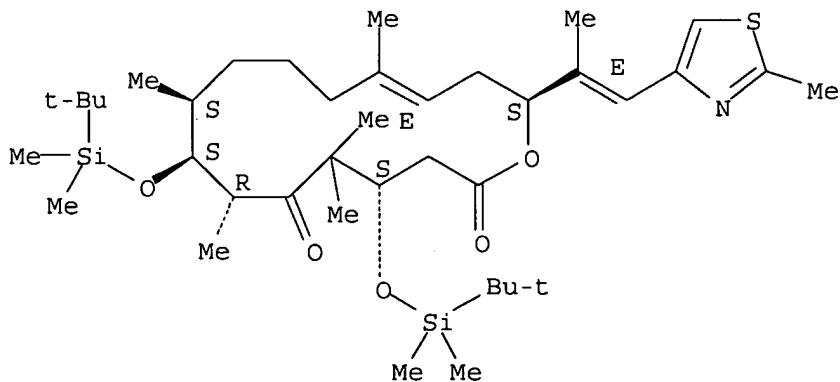


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN  
 ITERATION INCOMPLETE

IN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethyl-2-methyl-4-thiazolyl)ethenyl]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI)  
 MF C39 H69 N O5 S Si2

Absolute stereochemistry. Rotation (-).  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN  
 ITERATION INCOMPLETE

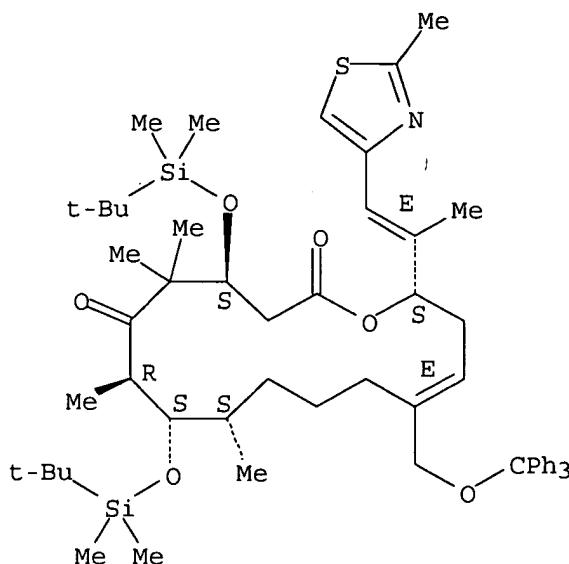
IN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-

10/004, 571R>

dimethylethyl)dimethylsilyloxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(triphenylmethoxy)methyl]-,  
(4S,7R,8S,9S,13E,16S)- (9CI)

MF C58 H83 N O6 S Si2

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> s 11 ful  
FULL SEARCH INITIATED 17:06:50 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 1517 TO ITERATE

100.0% PROCESSED 1517 ITERATIONS ( 80 INCOMPLETE) 80 ANSWERS  
SEARCH TIME: 00.00.01

L3 80 SEA SSS FUL L1

=> file caplus  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
FULL ESTIMATED COST ENTRY SESSION  
161.76 161.97

FILE 'CAPLUS' ENTERED AT 17:06:59 ON 08 MAR 2005  
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FILE COVERS 1907 - 8 Mar 2005 VOL 142 ISS 11  
FILE LAST UPDATED: 7 Mar 2005 (20050307/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13  
L4 57 L3

=> s 14 (and process or prepar? or make or made or synthe?)  
MISSING OPERATOR 'L4 (AND'

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s 14 and (process or prepar? or make or made or synthe?)

2057964 PROCESS

1371858 PROCESSES

3060581 PROCESS

(PROCESS OR PROCESSES)

1532491 PREPAR?

114913 PREP

2021 PREPS

116735 PREP

(PREP OR PREPS)

1917417 PREPD

21 PREPDS

1917432 PREPD

(PREPD OR PREPDS)

105866 PREPG

12 PREPGS

105877 PREPG

(PREPG OR PREPGS)

2555437 PREPN

198549 PREPNS

2705847 PREPN

(PREPN OR PREPNS)

4484517 PREPAR?

(PREPAR? OR PREP OR PREPD OR PREPG OR PREPN)

205295 MAKE

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1137640 MADE

23 MADES

1137660 MADE

(MADE OR MADES)

1431845 SYNTHE?

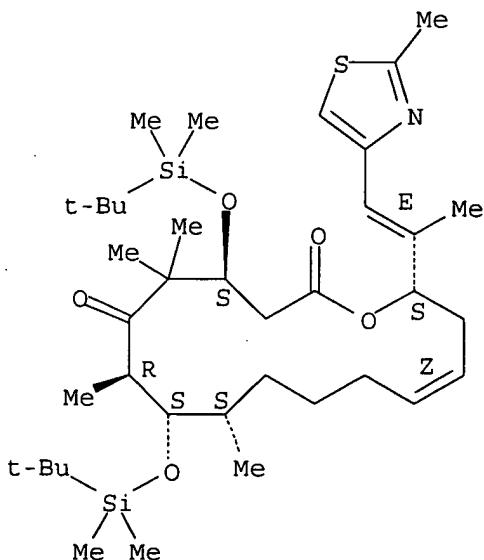
L5 57 L4 AND (PROCESS OR PREPAR? OR MAKE OR MADE OR SYNTHE?)

10/004,571R>

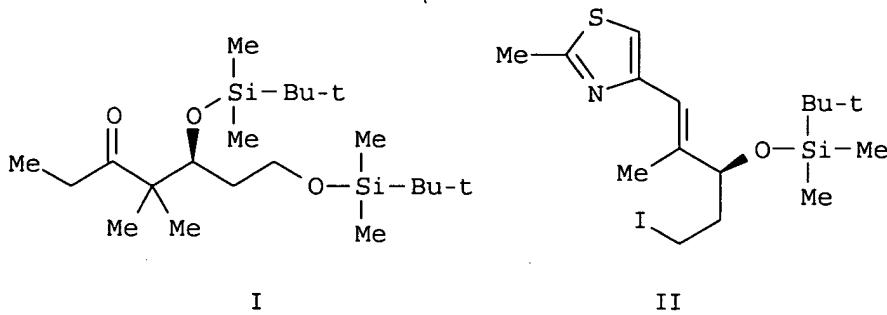
=> d 15 ibib hitstr abs 1-57

L5 ANSWER 1 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:454851 CAPLUS  
DOCUMENT NUMBER: 141:140221  
TITLE: Multi-step application of immobilized reagents and scavengers: A total **synthesis** of epothilone C  
AUTHOR(S): Storer, R. Ian; Takemoto, Toshiyasu; Jackson, Philip S.; Brown, Dearn S.; Baxendale, Ian R.; Ley, Steven V.  
CORPORATE SOURCE: Department of Chemistry, University of Cambridge, Cambridge, CB2 1EW, UK  
SOURCE: Chemistry--A European Journal (2004), 10(10), 2529-2547  
PUBLISHER: CODEN: CEUJED; ISSN: 0947-6539 Wiley-VCH Verlag GmbH & Co. KGaA  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 141:140221  
IT 186692-84-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(total **synthesis** of epothilone C via asym. **synthesis** and stereoselective coupling of heptanone, methylheptenal, and thiazole fragments using immobilized reagents and scavengers)  
RN 186692-84-2 CAPLUS  
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



GI



AB The total **synthesis** of the cytotoxic antitumor natural product epothilone C has provided a stage for the exploitation and further development of immobilized reagent methods. A stereoselective convergent synthetic strategy was applied, incorporating polymer-supported reagents, catalysts, scavengers and catch-and-release techniques to avoid frequent aqueous work-up and chromatog. purification. The enantioselective **preparation** of 3 key fragments heptanone I, (S)-2-methyl-6-heptenal, and thiazole II along with their elaboration via diastereoselective coupling into epothilone C is presented.

REFERENCE COUNT: 122 THERE ARE 122 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:106102 CAPLUS

DOCUMENT NUMBER: 140:357084

TITLE: Rapid access to epothilone analogs via semisynthetic degradation and reconstruction of epothilone D

AUTHOR(S): Dong, Steven D.; Sundermann, Kurt; Smith, Karen M. J.; Petryka, Joseph; Liu, Fenghua; Myles, David C.

CORPORATE SOURCE: Department of Chemistry, Kosan Biosciences, Hayward, CA, 94545, USA

SOURCE: Tetrahedron Letters (2004), 45(9), 1945-1947

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 189453-35-8P

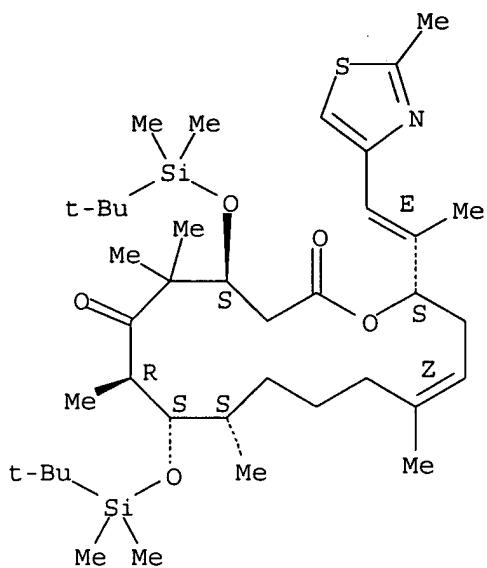
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of epothilone D analogs via semisynthetic degradation and ring-closing metathesis and their antitumor activity)

RN 189453-35-8 CAPLUS

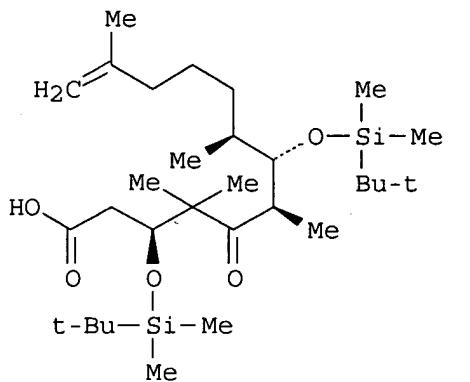
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[((1,1-dimethylethyl)dimethylsilyl)oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



GI



I

AB A facile and efficient route to epothilone analogs has been developed from the natural product epothilone D (I). Degradation of I via an oxidative cleavage sequence provides acid intermediate II rapidly in six steps. From II, a variety of epothilone analogs have been **prepared** utilizing ring-closing metathesis to reconstruct the trisubstituted-12,13-double bond. Using this approach, we report a number of epothilone analogs with varying C-15 aromatic side chains and C-14 allylic substitutions and their antitumor activities.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:986626 CAPLUS

DOCUMENT NUMBER: 141:379

TITLE: Conformation-activity relationships in polyketide natural products. Towards the biologically active conformation of epothilone

AUTHOR(S): Taylor, Richard E.; Chen, Yue; Galvin, Gabriel M.; Pabba, Praveen K.

CORPORATE SOURCE: Department of Chemistry & Biochemistry and the Walther Cancer Research Center, University of Notre Dame, Notre Dame, IN, 46556-5670, USA

SOURCE: Organic & Biomolecular Chemistry (2004), 2(1), 127-132

CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:379

IT 746637-22-9P

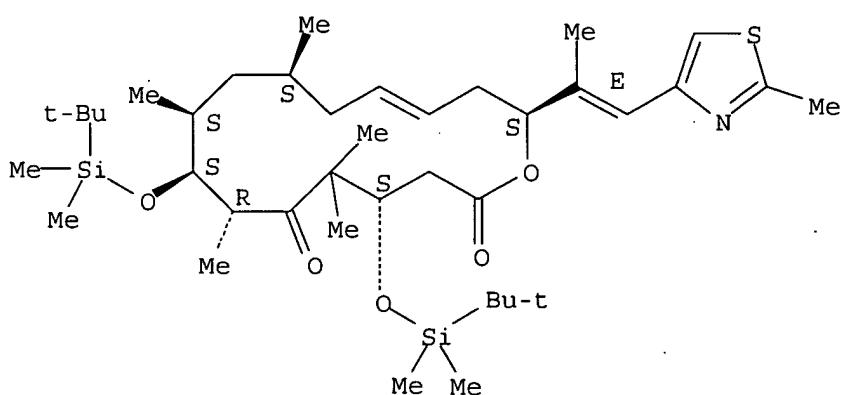
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (conformation-activity relationships in polyketide natural products reveals biol. active conformation of epothilone)

RN 746637-22-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,11-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,11S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as described by E or Z.



AB The conformation-activity relationships for the biol. active polyketide, epothilone, have been determined. Computer-based mol. modeling and high field NMR techniques have provided the solution preferences for epothilones 1 and 2. For the C1-C8 polypropionate region, two conformational families, conformers 1 and 2, have been identified as having significant populations in polar and non-polar solvents. In the C11-C15 region, addnl. flexibility was observed and two local conformations have been identified as important, conformers 3 and 4. Epothilone analogs with altered conformational profiles have been designed and synthesized. Conformational anal. and the results of biol. assays have been correlated to provide increased understanding of the biol. active conformation for the epothilone class of natural product. Conformation-activity relationships have been shown to be an important complement to structure-activity data.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

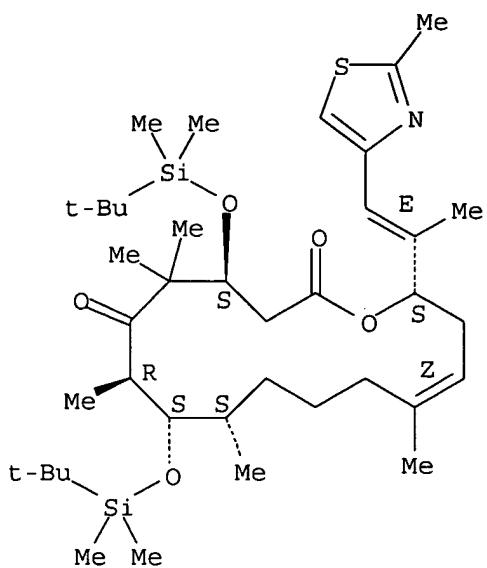
L5 ANSWER 4 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

10/004,571R>

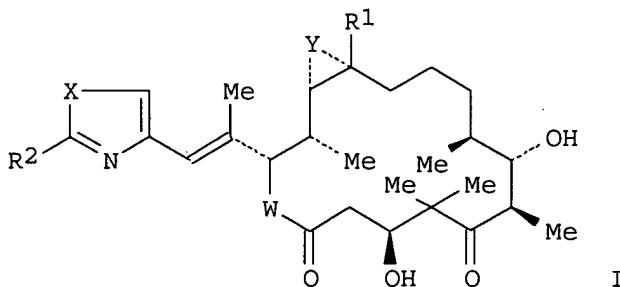
ACCESSION NUMBER: 2003:434313 CAPLUS  
DOCUMENT NUMBER: 139:22063  
TITLE: Preparation of 14-methylepothilones for therapeutic use in treatment of cancer and other diseases or conditions characterized by cellular hyperproliferation  
INVENTOR(S): Myles, David; Sundermann, Kurt; Dong, Steven  
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA  
SOURCE: PCT Int. Appl., 70 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045324	A2	20030605	WO 2002-US37945	20021126
WO 2003045324	A3	20040415		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW		
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
US 2003134883	A1	20030717	US 2002-304315	20021126
PRIORITY APPLN. INFO.:			US 2001-333465P	P 20011126
OTHER SOURCE(S):	MARPAT	139:22063		
IT 189453-35-8P	RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)	(preparation of 14-methylepothilones for therapeutic use in treatment of cancer and other diseases and conditions characterized by undesired cellular hyperproliferation)		
RN 189453-35-8	CAPLUS			
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)				

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



GI



AB 14-Methylepothilone compds., such as I [R1 = H, alkyl; R2 = CH<sub>2</sub>OH, CH<sub>2</sub>NH<sub>2</sub>, alkyl; W = O, NH; X = S, O; Y = O, bond], were prepared for use in treatment of cancer and other diseases and conditions characterized by undesired cellular hyperproliferation. Thus, (14S)-14-Methylepothilone D I (R1 = R2 = Me, W = O, X = S, Y = bond) was prepared via a multistep synthetic sequence which included a metathesis/macrocyclization step. The prepared 14-methylepothilones were assayed for activity against several cell lines, such as MCF-7, NCI-ADR and H460.

L5 ANSWER 15 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:157050 CAPLUS

DOCUMENT NUMBER: 136:216592

TITLE: Procedures for the production of 12,13-cyclopropylepothilone derivatives, as well as for their use in pharmaceutical preparations

PATENT ASSIGNEE(S): Schering Ag, Germany

SOURCE: Ger. Offen., 64 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

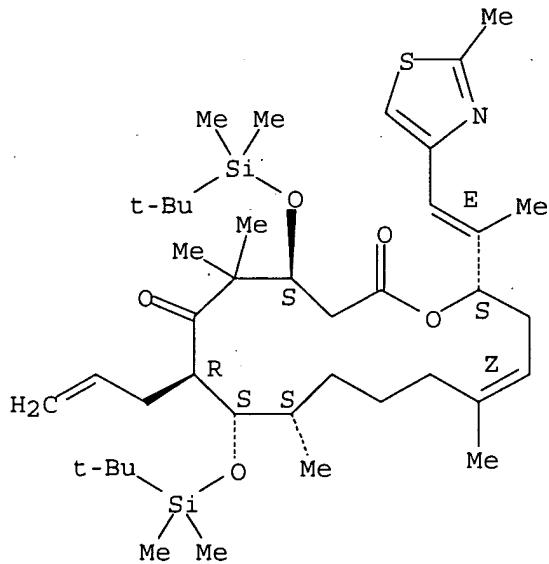
FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10041470	A1	20020228	DE 2000-10041470	20000818
PRIORITY APPLN. INFO.:			DE 2000-10041470	20000818
OTHER SOURCE(S):	CASREACT 136:216592; MARPAT 136:216592			
IT 305840-23-7P 305840-28-2P	RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)		(preparation of 12,13-cyclopropylepothilone derivs. and their use in pharmaceutical compns.)	
RN 305840-23-7 CAPLUS				
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,9,13-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-7-(2-propenyl)-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)				

Absolute stereochemistry.

Double bond geometry as shown.

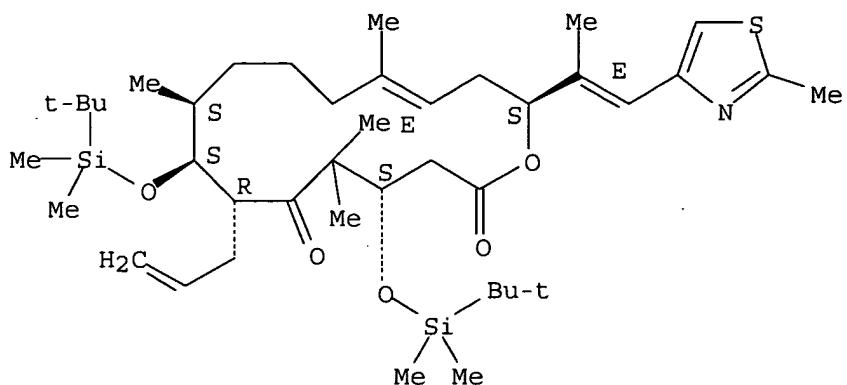


RN 305840-28-2 CAPLUS

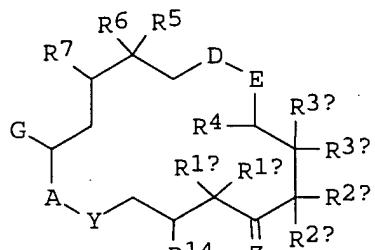
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,9,13-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-7-(2-propenyl)-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

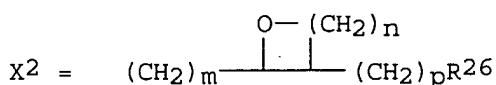
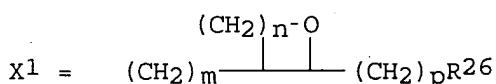
Double bond geometry as shown.



GI



I



**AB** The present invention describes new 6-alkenyl- and 6-alkynylepothilone derivs., e.g., I [R1a, R1b = H, C<sub>1</sub>-10-alkyl, aryl, C<sub>7</sub>-20-aralkyl; R1aR1b = (CH<sub>2</sub>)<sub>r</sub>, CH<sub>2</sub>OCH<sub>2</sub>; r = 1 - 5; R2a = H, C<sub>1</sub>-10-alkyl, aryl, C<sub>7</sub>-20-aralkyl, (CH<sub>2</sub>)<sub>m</sub>-C.tpbond.C-(CH<sub>2</sub>)<sub>p</sub>R<sup>26</sup>, (CH<sub>2</sub>)<sub>m</sub>-C:C-(CH<sub>2</sub>)<sub>p</sub>R<sup>26</sup>, X<sub>1</sub>, X<sub>2</sub>; n = 0 - 5; p = 0 - 3; m = 0 - 4; R2b = (CH<sub>2</sub>)<sub>m</sub>-C.tpbond.C-(CH<sub>2</sub>)<sub>p</sub>R<sup>26</sup>, (CH<sub>2</sub>)<sub>m</sub>-C:C-(CH<sub>2</sub>)<sub>p</sub>R<sup>26</sup>, X<sub>1</sub>, X<sub>2</sub>; R3a = H, C<sub>1</sub>-10-alkyl, aryl, C<sub>7</sub>-20-aralkyl; R3b = O-protecting group; R4 = H, C<sub>1</sub>-10-alkyl, aryl, C<sub>7</sub>-20-aralkyl, halogen, OH, O-protecting group, CN; R5 = H, C<sub>1</sub>-10-alkyl, aryl, C<sub>7</sub>-20-aralkyl, (CH<sub>2</sub>)<sub>s</sub>-T; S = 1 - 4; T = OH, O-protecting group, halogen; R6R7 = C(R<sup>33</sup>)<sub>2</sub>, NR<sup>32</sup> AY = OC(:O), OCH<sub>2</sub>, CH<sub>2</sub>C(:O), NR<sup>29</sup>SO<sub>2</sub>; DE = CH<sub>2</sub>CH<sub>2</sub>, CH<sub>2</sub>O, OCH<sub>2</sub>; G = X:CR<sub>8</sub>-; X = O, (O-alkyl)<sub>2</sub>, etc.; Z = H, H, OH, H, O-protective group; R8 = H, halogen, CN, C<sub>1</sub>-20-alkyl, aryl, C<sub>7</sub>-20-aralkyl; R14 = H, OH, halogen, O-SO<sub>2</sub>-alkyl, O-SO<sub>2</sub>-aryl, O-SO<sub>2</sub>-aralkyl; R26 = H, C<sub>1</sub>-10-alkyl, aryl, C<sub>7</sub>-20-aralkyl, C<sub>1</sub>-10-acyl, OH,

O-protecting group; R29 = H, C1-20-alkyl; R32 = H, C1-4-alkyl, C1-4-acyl; R33 = H, halogen], which interact with tubulins by stabilizing the formed microtubulins (no data). I are able specifically to affect cell division and are suitable, for example for the treatment of malignant tumors ovarian -, stomach -, colon -, adeno -, chest -, lungs -, head and neck carcinoma, malignant melanoma, acute lymphocytic and myelocytic leukemia. In addition I are suitable for the anti-angiogenesis therapy as well as for the treatment of chronic ignitable illnesses (psoriasis, arthritis). For the avoidance of uncontrolled cell rampant growths on as well as the better compatibility of medical implants I can be up and/or brought into polymers materials. According to invention, I can be used alone or for the achievement of additive or synergistic effects in combination with further principles and substance classes applicable in the tumor therapy. Exptl. data from patents PCT/EP00/01333 and PCT/IB00/00657 are reproduced here.

L5 ANSWER 16 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:11427 CAPLUS

DOCUMENT NUMBER: 136:279243

TITLE: Alkyne metathesis: development of a novel molybdenum-based catalyst system and its application to the total **synthesis** of epothilone A and C  
Furstner, Alois; Mathes, Christian; Lehmann, Christian W.

AUTHOR(S): Furstner, Alois; Mathes, Christian; Lehmann, Christian W.

CORPORATE SOURCE: Max-Planck-Institut fur Kohlenforschung, Mulheim/Ruhr, 45470, Germany

SOURCE: Chemistry--A European Journal (2001), 7(24), 5299-5317  
CODEN: CEUJED; ISSN: 0947-6539

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:279243

IT 186692-84-2P

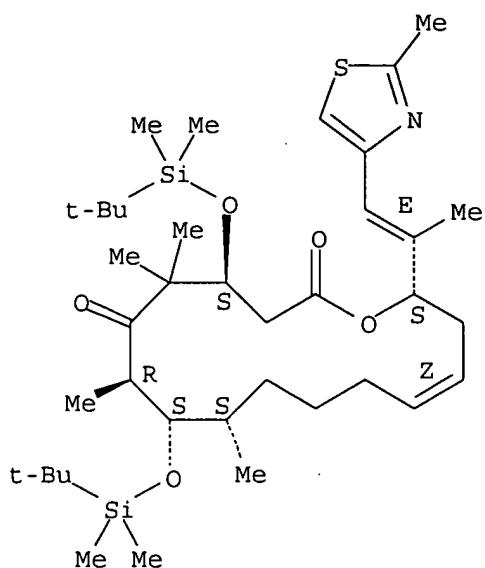
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(alkyne metathesis, development of a novel molybdenum-based catalyst system and its application to the total **synthesis** of epothilone A and C)

RN 186692-84-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Sterically hindered molybdenum(III) amido complexes of the general type  $[\text{Mo}\{\text{(tBu)(Ar)N}\}_3]$ , e.g. I, upon treatment with  $\text{CH}_2\text{Cl}_2$  or other halogen donors, have been converted into highly effective catalysts for all kinds of alkyne metathesis reactions. Although the actual nature of the propagating species formed *in situ* is still elusive, halogen transfer to the Mo center of I plays a decisive role in the activation of such precatalysts. It was possible to isolate and characterize by X-ray crystallog. some of the resulting molybdenum halide derivs. such as II ( $R = \text{OMe}$ ,  $X = \text{Cl}$ ), II ( $R = \text{Me}$ ,  $X = \text{Cl}$ ) and III which themselves were shown to be catalytically active. Numerous applications illustrate the performance of the catalytic system I/ $\text{CH}_2\text{Cl}_2$  which operates under mild conditions and tolerates an array of polar functional groups. The wide scope allows the method to be implemented into the total **synthesis** of sensitive and polyfunctional natural products. Most notable among them is a concise entry into the potent anticancer agents epothilone A and C. The macrolide core of these targets is forged by ring closing alkyne metathesis (RCAM) of diyne IV, followed by Lindlar hydrogenation of the resultant cycloalkyne thus formed. Since this strategy opens a stereoselective entry into ( $Z$ )-alkene V, the approach is inherently more efficient than previous **syntheses** based on conventional RCM.

REFERENCE COUNT: 169 THERE ARE 169 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 26 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:138738 CAPLUS

DOCUMENT NUMBER: 134:311010

TITLE: Synthetic epothilone analogs with modifications in the

AUTHOR(S): northern hemisphere and the heterocyclic side-chain-  
**synthesis** and biological evaluation  
 End, Nicole; Bold, Guido; Caravatti, Giorgio;  
 Wartmann, Markus; Altmann, Karl-Heinz  
 TA Oncology Research, Novartis Pharma AG, Basel,  
 CH-4002, Switz.

CORPORATE SOURCE: Proceedings of ECSOC-3, [and] Proceedings of ECSOC-4,  
 Sept. 1-30, 1999 and 2000 (2000), Meeting Date  
 1999-2000, 1431-1442. Editor(s): Pombo-Villar,  
 Esteban. Molecular Diversity Preservation  
 International: Basel, Switz.

SOURCE: Conference; (computer optical disk)

DOCUMENT TYPE: Conference; (computer optical disk)

LANGUAGE: English

OTHER SOURCE(S): CASREACT 134:311010

IT 188260-22-2P

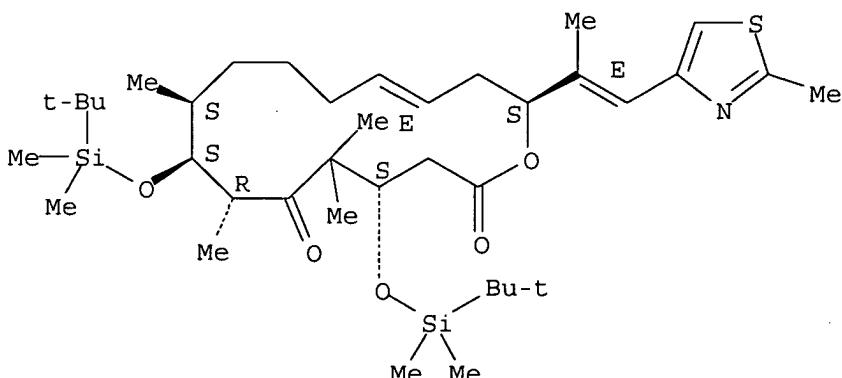
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (synthetic epothilone analogs with modifications in the northern  
 hemisphere and the heterocyclic side-chain-**synthesis** and  
 biol. evaluation)

RN 188260-22-2 CAPLUS

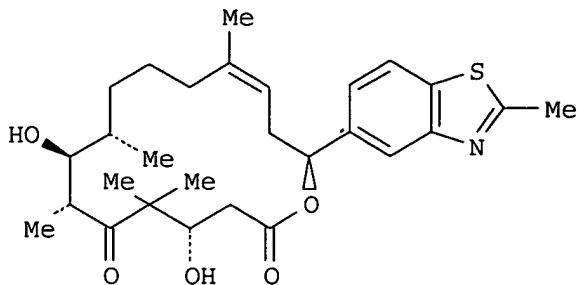
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



GI



AB The authors have **synthesized** epothilone analogs, e.g. I, with modifications in the northern hemisphere and the heterocyclic side-chain. In all three cases the key steps for construction of the macrocyclic skeleton involve Yamaguchi macrolactonization, the build-up of the requisite seco-acid through aldol reaction between the C7-C15 aldehyde and the dianion of the O-protected C1-C6  $\beta$ -hydroxy acid fragment, and the assembly of the C7-C15 aldehyde through the appropriate type of Pd(0)-catalyzed coupling reaction. The IC<sub>50</sub> for growth inhibition of the KB-31 tumor cell line for I was 0.45 nM.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 33 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:254124 CAPLUS  
 DOCUMENT NUMBER: 132:293600  
 TITLE: An efficient procedure for the **synthesis** of epothilone B, derivatives, and its intermediates  
 INVENTOR(S): Mulzer, Johann; Mantoulidis, Andreas; Oehler, Elisabeth  
 PATENT ASSIGNEE(S): Schering A.-G., Germany  
 SOURCE: Ger. Offen., 32 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19848306	A1	20000420	DE 1998-19848306	19981014
CA 2346493	AA	20000427	CA 1999-2346493	19991014
WO 2000023452	A1	20000427	WO 1999-EP7746	19991014
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964717	A1	20000508	AU 1999-64717	19991014
AU 763717	B2	20030731		
EP 1121364	A1	20010808	EP 1999-952569	19991014

EP 1121364	B1	20030108		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527521	T2	20020827	JP 2000-577178	19991014
AT 230751	E	20030115	AT 1999-952569	19991014
PT 1121364	T	20030430	PT 1999-952569	19991014
ES 2189508	T3	20030701	ES 1999-952569	19991014
US 6605726	B1	20030812	US 2001-807370	20010601
US 2003220503	A1	20031127	US 2003-420716	20030423
PRIORITY APPLN. INFO.:			DE 1998-19848306	A 19981014
			WO 1999-EP7746	W 19991014
			US 2001-807370	A3 20010601

OTHER SOURCE(S): CASREACT 132:293600; MARPAT 132:293600

IT 189453-35-8P

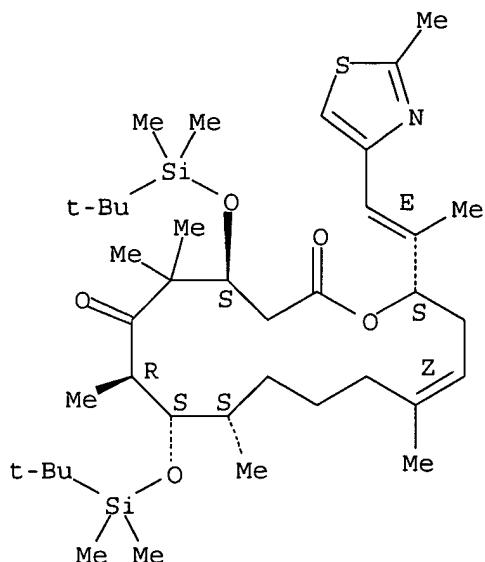
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis of epothilone B, derivs., and its intermediates)

RN 189453-35-8 CAPLUS

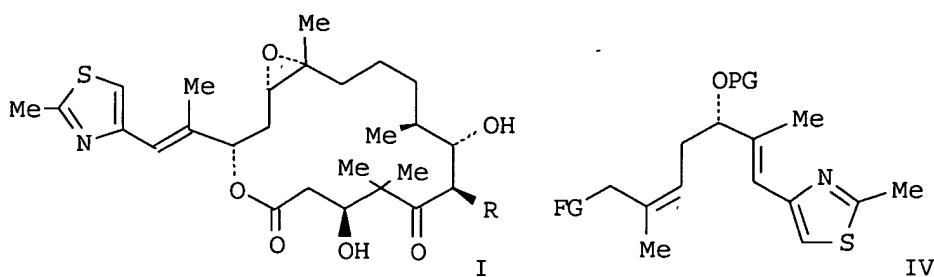
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[((1,1-dimethylethyl)dimethylsilyl)oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Double bond geometry as shown.



GI

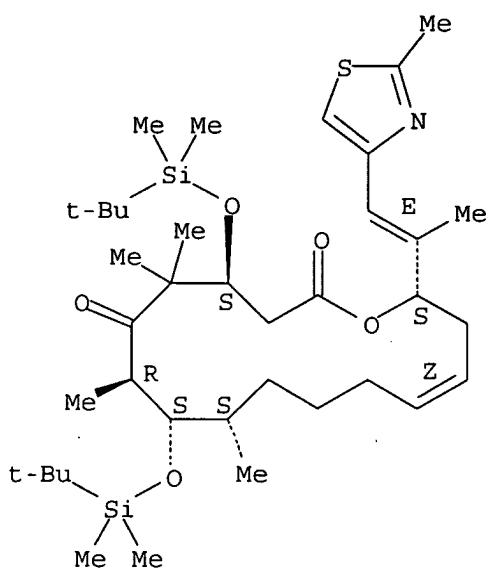


AB A new procedure for the production of epothilone B and its derivs. (I) ( $R =$  alkyl, cycloalkyl, aryl, heteroaryl, methylaryl, etc.) including its intermediates is reported. The method is based upon the stereoselective synthesis of three key structural fragments, C1-C6 (II) ( $S$ )-PGO( $CH_2$ ) $2CH(OPG)CMe_2COCH_2R$ , C7-C10 (III) ( $S$ )-PGO $CH_2CH(Me)CH_2CH_2FG$ , (PG = hydroxyl protecting group, such as TBDMs, etc. ; FG = SO $_2$ Ph, I, etc.), and C11-C20 (IV) starting with D-valine, TBDPS protected (2S)-methylpropan-1,3-diol and (S)-3-hydroxybutyrolactone, resp. The product, obtained after coupling of III and IV, on reaction with II formed an intermediate which on macrocyclization produced I.

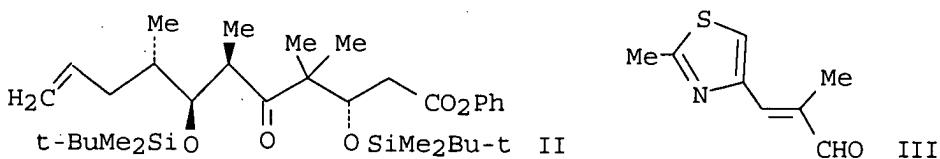
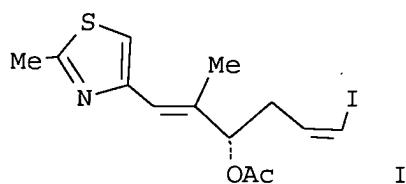
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2000:52387 CAPLUS  
DOCUMENT NUMBER: 132:251011  
TITLE: Enantioselective total **synthesis** of epothilone A using multifunctional asymmetric catalyses  
AUTHOR(S): Sawada, Daisuke; Shibasaki, Masakatsu  
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, 113-0033, Japan  
SOURCE: Angewandte Chemie, International Edition (2000), 39(1), 209-213  
CODEN: ACIEF5; ISSN: 1433-7851  
PUBLISHER: Wiley-VCH Verlag GmbH  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 132:251011  
IT 186692-84-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(enantioselective total **synthesis** of epothilone A)  
RN 186692-84-2 CAPLUS  
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[((1,1-dimethylethyl)dimethylsilyl)oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



GI



AB The enantioselective total **synthesis** of epothilone A was achieved via the catalytic coupling of I and II. The key step in the **preparation** of I was the catalytic cyanosilylation of III. II was **prepared** via a catalytic organic acetalization followed by an aldol reaction.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:15195 CAPLUS

DOCUMENT NUMBER: 132:64110

## TITLE: The preparation process,

intermediate products and pharmaceutical use of epothilone derivatives

INVENTOR(S) : Buchmann, Bernd; Klar, Ulrich; Skuballa, Werner;  
 Schwede, Wolfgang; Schirner, Michael; Menrad, Andreas  
 PATENT ASSIGNEE(S) : Schering A.-G., Germany  
 SOURCE: PCT Int. Appl., 86 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000485	A1	20000106	WO 1999-EP4915	19990630
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19830060	A1	20000210	DE 1998-19830060	19980630
DE 19923001	A1	20001116	DE 1999-19923001	19990513
AU 9950369	A1	20000117	AU 1999-50369	19990630
PRIORITY APPLN. INFO.:			DE 1998-19830060	A 19980630
			DE 1999-19923001	A 19990513
			WO 1999-EP4915	W 19990630

OTHER SOURCE(S) : CASREACT 132:64110; MARPAT 132:64110

IT 253448-16-7P 253448-18-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

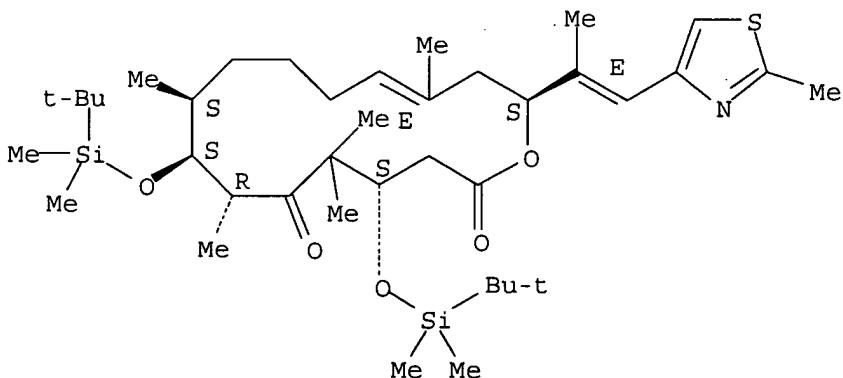
(preparation and pharmaceutical use of epothilone derivs.)

RN 253448-16-7 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[ (1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as described by E or Z.

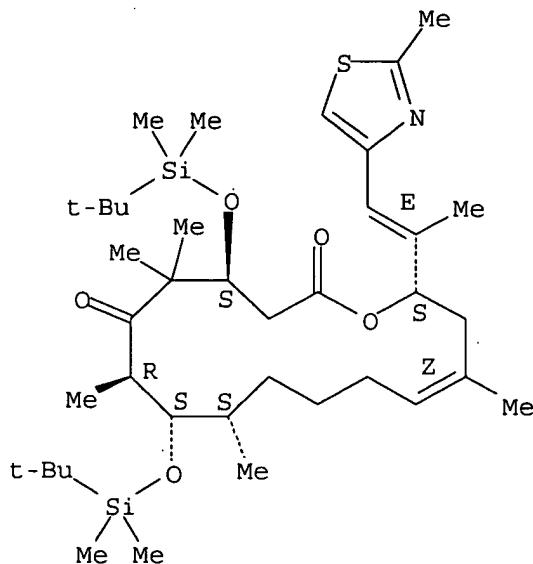


RN 253448-18-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[(1,1-

dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to new epothilone derivs. I [R1a, R1b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R1aR1b = (CH<sub>2</sub>)<sub>m</sub>, m = 2 - 5; R2a, R2b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R2aR2b = (CH<sub>2</sub>)<sub>n</sub>, n = 2 - 5; R3 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4a, R4b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4aR4b = (CH<sub>2</sub>)<sub>m</sub>, m = 2 - 5; D-E = CH<sub>2</sub>CH<sub>2</sub>, CH:CH, C.tplbond.C, oxirane ring, CH(OH)CH(OH), CH(OH)CH<sub>2</sub>; R5 = C1-10-alkyl, aryl, C7-10-aralkyl; R6, R7 = H; R6R7 = O, bond; R8 = C1-10-alkyl, aryl, C7-10-aralkyl; R25 = H, C1-10-alkyl, C1-10-hydroxyalkyl, C1-10-haloalkyl; X = O, (OR<sub>9</sub>)<sub>2</sub>, C<sub>2</sub>-10-alkylene- $\alpha$ , $\omega$ -dioxy, CR<sub>11</sub>R<sub>12</sub>; CX = CH(OR<sub>10</sub>); R9 = C1-20-alkyl; R10 = H, protecting group; R11, R12 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R11R12 = CH<sub>2</sub>, C<sub>5</sub>-7-carbocyclic ring; Y = O, CY = CH<sub>2</sub>; CZ = CH(OR<sub>13</sub>), R13 = H, protecting group] which are prepared via cyclization of ketones II [R15 = H, OH halogen, OR<sub>15a</sub>, OSO<sub>2</sub>R<sub>15b</sub>; R15a = H, SO<sub>2</sub>-alkyl, SO<sub>2</sub>-aryl, SO<sub>2</sub>-aralkyl, (CH<sub>2</sub>)<sub>o</sub>, CR<sub>16a</sub>R<sub>16b</sub>; R15b = H, C1-20-alkyl, aryl, C7-20-aralkyl; R16a, R16b = H, C1-10-alkyl, aryl, C7-20-aralkyl; R16aR16b = (CH<sub>2</sub>)<sub>q</sub>; o = 2 - 4; q = 3 - 6]. Thus, epothilone derivative III was prepared via macrolactonization of carboxylic acid IV with 2,4,6-trichlorobenzoyl chloride and Et<sub>3</sub>N in THF followed by deprotection with aqueous CF<sub>3</sub>CO<sub>2</sub>H in CH<sub>2</sub>Cl<sub>2</sub>. I cooperate with tubulin by stabilizing formed microtubuli.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

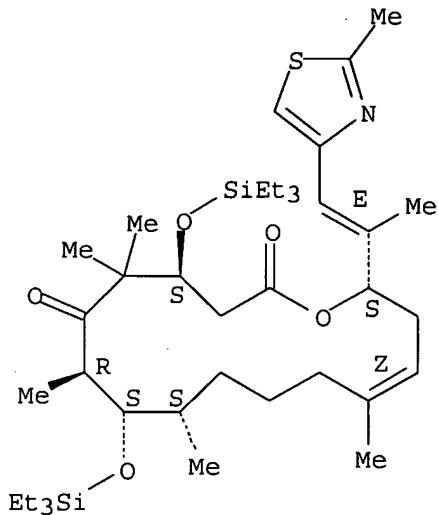
10/004,571R>

L5 ANSWER 36 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1999:691091 CAPLUS  
DOCUMENT NUMBER: 131:310502  
TITLE: synthesis and cytotoxicity of 12,13-modified epothilone derivatives for use in treatment of tumors or other hyperproliferative cellular disease  
INVENTOR(S): Vite, Gregory D.; Kim, Soong-Hoon Kim; Hofle, Gerhard  
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
SOURCE: PCT Int. Appl., 89 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

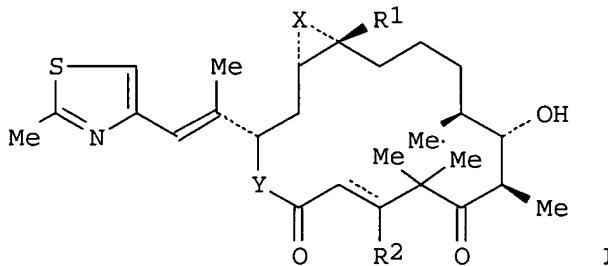
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954319	A1	19991028	WO 1999-US7475	19990405
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG				
US 6380395	B1	20020430	US 1999-280192	19990329
US 6399638	B1	20020604	US 1999-280191	19990329
CA 2329181	AA	19991028	CA 1999-2329181	19990405
AU 9934716	A1	19991108	AU 1999-34716	19990405
AU 748526	B2	20020606		
BR 9909795	A	20001226	BR 1999-9795	19990405
TR 200003036	T2	20010122	TR 2000-200003036	19990405
EP 1073648	A1	20010207	EP 1999-916383	19990405
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002512239	T2	20020423	JP 2000-544658	19990405
PRIORITY APPLN. INFO.:			US 1998-82564P	P 19980421
			WO 1999-US7475	W 19990405

OTHER SOURCE(S): MARPAT 131:310502  
IT 247230-54-2P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis and cytotoxicity of 12,13-modified epothilone derivs. for use in treatment of tumors or other hyperproliferative cellular disease)  
RN 247230-54-2 CAPLUS  
CN Oxacyclohexadec-13-ene-2,6-dione, 5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



GI



AB    **Synthesis** and cytotoxicity of 12,13-modified epothilone derivs. (I) [R1 = H, (un)substituted alkyl; R2 = H if bond double or BOH if bond single; Y = O, NH; X = O, (un)substituted NH, OCH<sub>2</sub>, 2-methylthiazolo, S, (un)substituted CH<sub>2</sub>] is presented. Thus, I (R1 = H, X = NH, R2 = BOH, Y = O) (II) is **prepared** by epoxidn. of epothilone C followed by azidation and reductive imination. I are useful in treatment of tumors or other hyperproliferative cellular disease and show IC<sub>50</sub> of 0.01-1000 nM in cell proliferation tests.

REFERENCE COUNT:                2                THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 45 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:                1998:492150 CAPLUS

DOCUMENT NUMBER:                129:216449

TITLE:                          Total **synthesis** of (-)-epothilone B

AUTHOR(S):                      May, Scott A.; Grieco, Paul A.

CORPORATE SOURCE:              Department of Chemistry and Biochemistry, Montana State University, Bozeman, MT, 59717, USA

SOURCE:                         Chemical Communications (Cambridge) (1998), (15), 1597-1598

CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER:                     Royal Society of Chemistry

10/004,571R>

DOCUMENT TYPE: Journal  
LANGUAGE: English

IT 204195-20-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

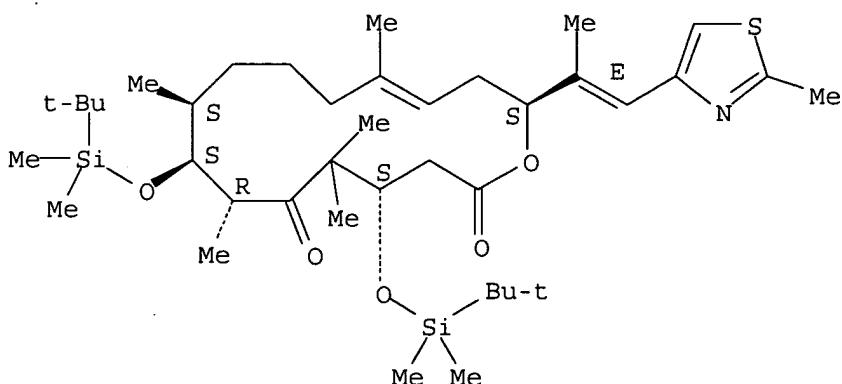
(total synthesis of (-)-epothilone B)

RN 204195-20-0 CAPLUS

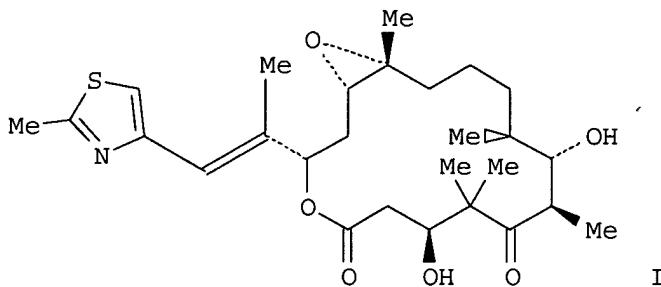
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[((1,1-dimethylethyl)dimethylsilyl)oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as described by E or Z.



GI



AB The sixteen-membered ring macrolide (-)-epothilone B (I) has been synthesized by a route which features stereospecific methylation of an (E)- $\gamma$ ,8-epoxy acrylate, the use of a double asym. reaction employing (R,R)-diisopropyltartrate and (E)-crotylboronate, ring closure by means of an olefin metathesis reaction.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 53 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1997:302059 CAPLUS

DOCUMENT NUMBER: 127:4948  
 TITLE: Total synthesis of (-)-epothilone B: an extension of the Suzuki coupling method and insights into structure-activity relationships of the epothilones  
 AUTHOR(S): Su, Dai-Shi; Meng, Dongfang; Bertinato, Peter; Balog, Aaron; Sorensen, Erik J.; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.  
 CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA  
 SOURCE: Angewandte Chemie, International Edition in English (1997), 36(7), 757-759  
 CODEN: ACIEAY; ISSN: 0570-0833  
 PUBLISHER: VCH  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 127:4948

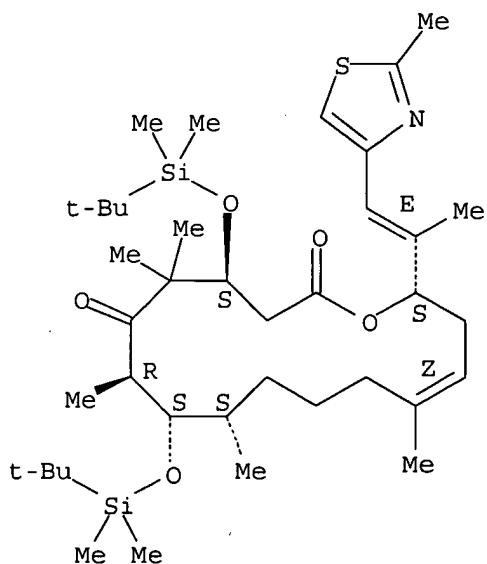
IT 189453-35-8P 189453-54-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis of epothilone B via a Suzuki coupling and insights into antitumor structure-activity relationships)

RN 189453-35-8 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

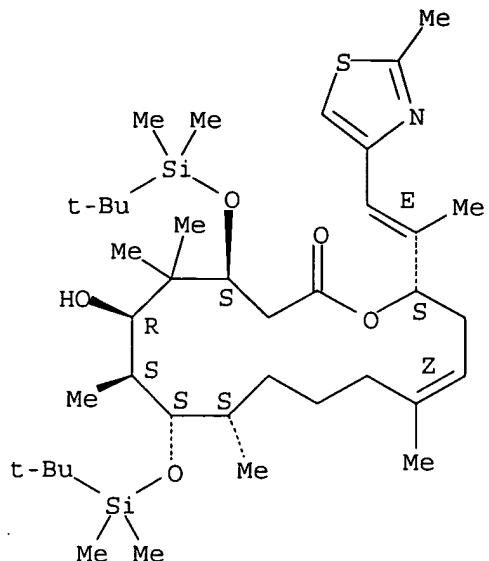
Absolute stereochemistry. Rotation (-).  
 Double bond geometry as shown.



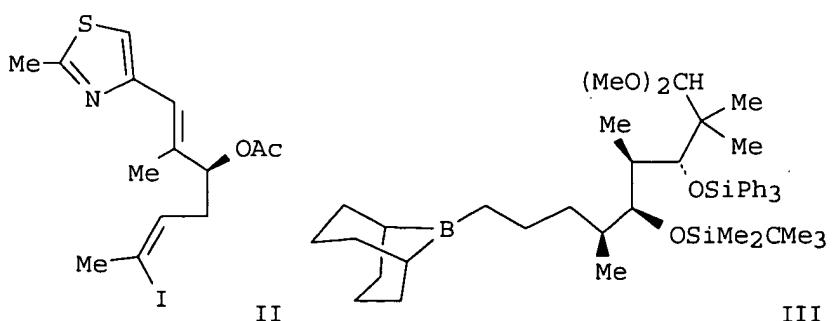
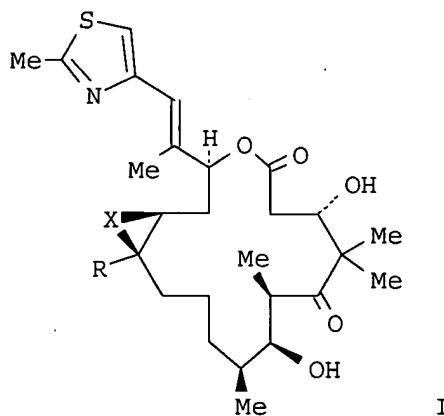
RN 189453-54-1 CAPLUS

CN Oxacyclohexadec-13-en-2-one, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,6R,7S,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



GI



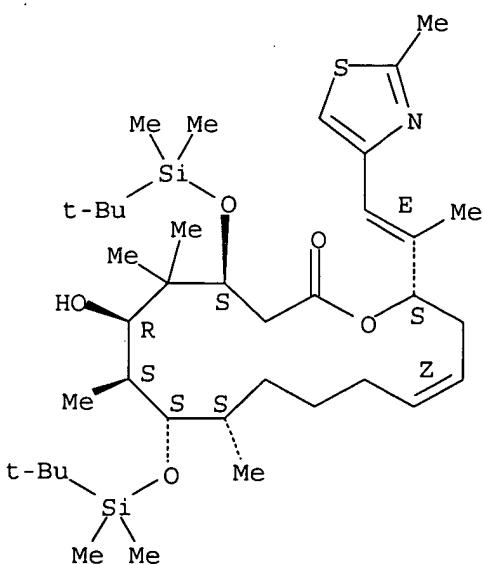
AB     (-)-Epothilone B (I; R = Me, X = O) and desoxyepothilone B (I; R = Me, X =

bond) were prepared via Suzuki coupling of (*Z*)-vinyl iodide II with borane III. I (R = H, Me, X = O, bond) and the E-isomers of I (R = H, Me, X = bond) were tested for efficacy against drug-sensitive and resistant CCRF-CEM cell lines (IC<sub>50</sub> = 0.0004 - 0.262 μM).

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 57 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1997:72321 CAPLUS  
 DOCUMENT NUMBER: 126:144023  
 TITLE: Total synthesis of (-)-epothilone A  
 AUTHOR(S): Balog, Aaron; Meng, Dongfang; Kamenecka, Ted;  
 Bertinato, Peter; Su, Dai-Shi; Sorensen, Erik J.;  
 Danishefsky, Samuel J.  
 CORPORATE SOURCE: Lab. for Bioorganic Chemistry, Sloan-Kettering  
 Institute for Cancer Research, New York, NY, 10021,  
 USA  
 SOURCE: Angewandte Chemie, International Edition in English  
 (1997), Volume Date 1996, 35(23/24), 2801-2803  
 CODEN: ACIEAY; ISSN: 0570-0833  
 PUBLISHER: VCH  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 186692-83-1P 186692-84-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (total synthesis of (-)-epothilone A via a B-alkyl Suzuki  
 coupling followed by closure of the macrocycle with an aldol reaction)  
 RN 186692-83-1 CAPLUS  
 CN Oxacyclohexadec-13-en-2-one, 4,8-bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]  
 ]-6-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-  
 thiazolyl)ethenyl]-, (4S,6R,7S,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
 Double bond geometry as shown.

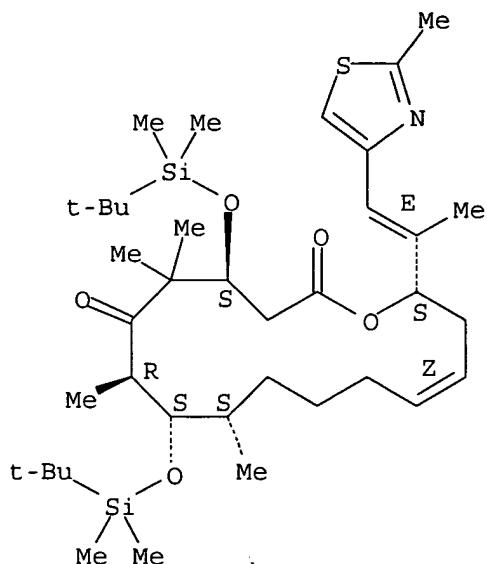


10/004,571R>

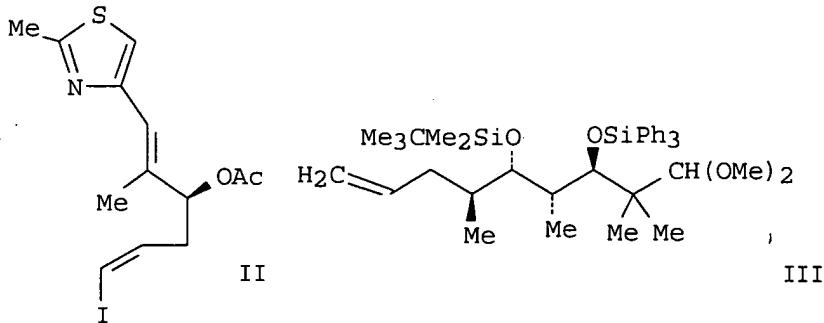
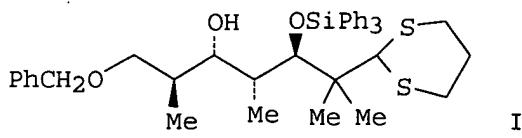
RN 186692-84-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).  
Double bond geometry as shown.



GI



AB (-)-Epothilone A was prepared from dithiane I, (R)-glycidol and [(2-methyl-1,3-thiazol-4-yl)methyl]diphenylphosphine oxide via a B-alkyl Suzuki coupling of thiazole II with acetal III followed by closure of the macrocycle with an aldol reaction.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/004,571R>

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-41.61	-41.61

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